It is claimed:

1. A method of identifying polymorphic DNA sequences in a test DNA population, the method comprising the steps of:

(a) providing a reference DNA population;

(b) forming a population of heteroduplexes from single stranded DNA of the reference DNA population and from single stranded DNA of the test DNA population;

(c) isolating mismatched heteroduplexes of the population by digesting a single stranded DNA of substantially every perfectly matched duplex;

(d) amplifying the isolated mismatched heteroduplexes to form a population of amplicons; and

(e) determining the nucleotide sequence of a portion of each amplicon so that polymorphic DNA sequences of the test DNA population are identified.

2. The method of claim 1 wherein the step of isolating further includes digesting said heteroduplexes with a single stranded exonuclease whose substrate is duplex DNA.

3. The method of claim 2 wherein said steps of providing said reference DNA population and said test DNA population include providing members of said reference DNA population in a first cloning vector and providing members of said test DNA population in a second cloning vector, the first cloning vector having a first primer binding site, a second primer binding site, a third primer binding site, and a cloning site disposed between the second and third primer binding sites.

4. The method of claim 3 wherein said second cloning vector has a fourth primer binding site, a fifth primer binding site, and a cloning site disposed between the fourth primer binding site and the fifth primer binding site, and the fifth primer binding site having a nucleotide sequence identical to said third primer binding site.

5. The method of claim 4 wherein said single stranded DNA of said reference DNA population is generated by amplifying said members of said reference DNA population in a polymerase chain reaction using a nuclease-resistant primer specific for said first primer binding site and a primer specific for said third primer binding site to form an amplicon having a single strand with a nuclease-resistant 5' end, and digesting the amplicon with a 5'→3' exonuclease.

6. The method of claim 5 wherein said single stranded DNA of said test DNA population is generated by amplifying said members of said test DNA population in a polymerase chain reaction using a nuclease-resistant primer specific for said fourth primer binding site and a primer specific for said fifth primer binding site to form an amplicon having a single strand with a nuclease-resistant 5' end, and digesting the amplicon with a 5'→3' exonuclease.

7. The method of claim 2 wherein said step of forming a population of heteroduplexes includes partitioning said test DNA population into subpopulations and separately forming subpopulations of heteroduplexes from single stranded DNA of said reference DNA population and single stranded DNA from each subpopulation of said test DNA population.

8. The method of claim 7 wherein said subpopulations of said test DNA population and said reference DNA population have complexities which permit at least ninety percent of heteroduplexes of said subpopulations of heteroduplexes to be formed in seventy-two hours or less.

9. A cloning vector for incorporation of DNA digested by a restriction endonuclease, the cloning vector comprising the following sequence of elements:

a first restriction endonuclease recognition site;

a stuffer fragment; and

a second restriction endonuclease recognition site, the first and second restriction endonuclease recognition sites being specific for restriction endonucleases selected from the set consisting of type IIs restriction endonucleases and type II restriction endonucleases recognizing interrupted palindromic sequences.

10. The cloning vector of claim 9 wherein said first restriction endonuclease recognition site and said second restriction endonuclease recognition site are the same.

11. The cloning vector of claim 10 wherein said first restriction endonuclease recognition site and said second restriction endonuclease recognition site are selected from the group consisting of Sap I, Ear I, Ksp632 I, Mwo I, Blp I, Bsu36I, Dde I, Hinf I, EcoO109 I, and Sau96 I.

12. A method of cloning a restriction fragment, the method comprising the steps of:

providing a population of restriction fragments, each end of each restriction fragment of the population having a recessed 3' strand and a protruding 5' strand, the protruding 5' strand having a predetermined palindromic sequence;

extending the recessed 3' strand by one nucleotide to form a modified end;

providing a cloning vector comprising a first restriction endonuclease recognition site, a stuffer fragment, and a second restriction endonuclease recognition site, the first and second restriction endonuclease recognition sites being specific for a restriction endonuclease selected from the set consisting of type IIs restriction endonucleases and type II restriction endonucleases recognizing interrupted palindromic sequences;

digesting the cloning vector with one or more restriction endonucleases that recognize the first and second restriction endonuclease recognition sites to form an opened cloning vector with ends complementary to the modified ends of the restriction fragment;

inserting the restriction fragment having modified ends into the opened cloning vector; and

transforming a host with the cloning vector carrying the inserted restriction fragment.

13. The method of claim 12 wherein said step of extending includes extending said recessed 3' strand with a DNA polymerase in the presence of a predetermined nucleoside triphosphate.

14. The method of claim 13 wherein said protruding 5' strand consists of four nucleotides.

15. The method of claim 14 wherein said restriction endonuclease recognizing said first and said second restriction endonuclease recognition sites is selected from the group consisting of Sap I, Ear I, Ksp632 I, and Mwo I.

16. The method of claim 15 wherein said restriction endonuclease recognizing said first and said second recognition sites is Sap I and said first and said second restriction endonuclease recognition sites are located with said stuffer fragment.